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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/023,441	12/18/2001	Martin J. Jacobs	CP216	2296

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EXAMINER	
MAIER, LEIGH C	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 05/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/023,441	JACOBS ET AL.	
	Examiner	Art Unit	
	Leigh C. Maier	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *10 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *49-87* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *49-87* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 1-48 have been canceled. Claims 49-87 were added. Claims 50-57, 59-82, 84, 86, and 87 were amended by supplemental amendment. Any objection or rejection not expressly repeated has been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The declaration under 37 CFR 1.132 filed 10 November 2003 is insufficient to overcome the rejection of claims 1-5, 9, 10, 12-19, 21, 24, 25, 28, 35-43, 46, and 48 (corresponding to newly submitted claims 49, 51, 52, 54, 57-59, 63-67, 69-73, 77, 78, and 81) based upon 35 U.S.C. § 102 as set forth in the last Office action for reasons set forth below.

Claim Rejections - 35 U.S.C. §102

Claims 49, 51, 52, 54, 57-59, 63-67, 71-73, 77, 78, and 81 are rejected under 35 U.S.C. 102(b) as being anticipated by RAMBERT et al (Neuropharmacology, 1994) with HEDGES (Chem. Rev., 1998) to support inherency, as applied to canceled claims 1-5, 9, 10, 12-19, 21, 24, 25, 28, 35-43, 46, and 48 in the previous Office action. Newly added claim 83 is also included in this rejection.

Applicant's arguments filed 10 November 2003 have been fully considered but they are not persuasive. Applicant relies on the contents of the Jacobs declaration to traverse this rejection. The declaration indicates that heating a solution of 2% HP–β–CD and 10 mg/ml of modafinil results in dissolution of the modafinil which precipitates upon cooling. The declaration

concludes that "modafinil is not fully solubilized at 10 mg/ml in an aqueous 2% hydroxy-propyl-betacyclodextrin (by weight) at room temperature." This is not persuasive because the claims contain no temperature limitation.

Newly submitted claim 83 is drawn to the preparation of an inclusion complex of a modafinil compounds and a CD wherein the modafinil has an aqueous solubility of 10 mg/ml comprising contacting the modafinil with the CD in an aqueous medium. RAMBERT is silent with regard to the details of the preparation of the disclosed solution. However, the solution is disclosed, and by definition, the modafinil contacts the CD in an aqueous solution.

Claim Rejections - 35 U.S.C. § 103

Claims 49-52, 54-67, 70-73, 77, 78, 81, and 83 are rejected under 35 U.S.C. 103(a) as being unpatentable over RAMBERT et al (Neuropharmacology, 1994) in view of PITHA et al (Int. J. Pharm., 1986) as applied to canceled claims 1-10, 12-19, 21-24, 28, 35-43, and 46-48 in the previous Office action.

Applicant's arguments filed 10 November 2003 have been fully considered but they are not persuasive. Applicant contends that the data presented in PITHA is insufficient to determine the molar ratio of active agent to CD. The examiner agrees that the reference is silent with respect to the density of a 50% solution of HP–β–CD which would allow for the precise determination of the molar ratios disclosed in the reference. However, one of ordinary skill could make reasonable approximations. For example, starting with an approximate molecular weight of about 1600 g/mol for HP–β–CD, if a 50% solution has a density of 1.0, a milliliter of the solution would comprise 500 mg or 313 mmol. This solution is likely to be more dense, so if the

density is 1.25, for example, it would comprise 625 mg or 391 mmol. Taking the modafinil concentrations 10 mg/ml and 20 mg/ml suggested by RAMBERT, these solutions comprise 37 mmol and 74 mmol of modafinil, respectively. A solution prepared from the combination of these references would provide molar ratios within the recited ranges. It would be within the scope of the artisan to optimize the ratios through routine experimentation.

Claim 84 is rejected under 35 U.S.C. 103(a) as being unpatentable over RAMBERT et al (Neuropharmacology, 1994) as applied to claims 49, 51, 52, 54, 57-59, 63-67, 69-73, 77, 78, 81, and 83 above, further in view of NGUYEN et al (US 5,843,347) and HEDGES (Chem. Rev., 1998).

Newly submitted claims 51 and 66 recite various species of cyclodextrins for use in preparing the inclusion complexes recited in claims 49 and 58, respectively. Claim 84 further limits the process described in claim 83 above, wherein the inclusion complex is dried and isolated as a solid.

RAMBERT teaches that HP–β–CD has utility for solubilizing modafinil as discussed in the previous Office action. The reference does not teach the full scope of recited cyclodextrins or the isolation of the inclusion complex by drying.

NGUYEN also teaches the preparation of a composition comprising modafinil and HP–β–CD comprising a drying step, as set forth in the previous Office action. The reference is silent with respect to inclusion complex formation, but the process used to prepare this composition is consistent with methods known in the art for the preparation of inclusion complexes. (See HEDGES citation in previous Office action.) The reference exemplifies only the

use of HP–β–CD but expressly suggests the use of a wide variety of known cyclodextrins in the products and clearly contemplates the use of any known cyclodextrin. See col 6, lines 50-64.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare the exemplified modafinil complex with any of the cyclodextrins suggested by the reference for the art-disclosed utility. One of ordinary skill would expect success in making this modification. It would be further obvious to isolate the inclusion complex by drying because NYUGEN had taught that the solid product has utility in pharmaceutical applications.

Applicant alleges without support that "Nyugen fails to disclose the formation of a modafinil/cyclodextrin complex." Arguments of counsel cannot take the place of evidence in the record. The formation of an inclusion complex is addressed above.

Applicant further argues that "the teachings suggest use of the cyclodextrin as a sugar derivative, not as a complexing agent." However, the inherent properties of a compound are not negated by a lack of description in the reference. HP–β–CD is known to be a solubilizing vehicle (i.e., form an inclusion complex) with modafinil. When combined with modafinil in a manner known to be useful for preparing inclusion complexes, such as slurrying followed by drying, one of ordinary skill would reasonably expect that an inclusion would be formed.

Claims 53, 68, 74-76, 79, 80, 82, and 85-87 are rejected under 35 U.S.C. 103(a) as being unpatentable over RAMBERT et al (Neuropharmacology, 1994) in view of NGUYEN et al (US 5,843,347) and HEDGES (Chem. Rev., 1998) as applied to claims 49, 51, 52, 54, 57-59, 63-67, 69-73, 77, 78, 81, 83, and 84 above, and further in view of GREBOW et al (US 5,618,845).

The invention is as set in the previous Office action and further discussed above. Dependents recite specific unit doses; the composition in the form of a tablet, capsule, syrup, or elixir; and therapeutic methods.

RAMBERT, NGUYEN, and HEDGES teach as set forth in the previous Office action. The references do not teach the use of the levorotatory form of modafinil; specific unit doses; the composition in the form of a tablet, capsule, syrup, or elixir; or therapeutic methods.

GREBOW teaches as set forth in the previous Office action. The reference teaches that the levorotatory form of modafinil for the treatment of a number of disorders, such as depression and hypersommnia. See col 1, lines 58-64.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare composition comprising an inclusion complex of modafinil and a CD for the preparation of tablets, capsules, syrups or elixirs for the administration to patients treatment of the disorders taught by GREBOW. The artisan would be motivated to use such a composition for the increased solubility that the CD confers upon modafinil. One of ordinary skill would reasonably expect success in using said composition for such treatment. It would be further obvious to prepare the composition in unit dosages of 100 mg or 200 mg, as these dosages were taught by GREBOW. It would be further obvious to use this composition to treat any any mammal, such as humans or rats. It would be further obvious to prepare these compositions using the levorotatory form for its art-disclosed utility.

Claims 85-87 are rejected under 35 U.S.C. 103(a) as being unpatentable over NGUYEN et al (US 5,843,347) in view of (1) LAFON (US 5,391,576); (2) SCAMMELL et al (US

6,455,588); OR (3) MILLER et al (US 6,346,548), as applied to canceled claims 32-34 in the previous Office action.

The invention is as set forth in the previous Office action.

Applicant's arguments filed 10 November 2003 have been fully considered but they are not persuasive.

Applicant contends that the supplemental references do not cure the deficiencies of NGUYEN. The alleged deficiencies have been addressed above. Applicant's arguments appear to be that NGUYEN does not explicitly describe inclusion complex formation, and that the composition includes other components. The examiner would note that the claims neither require the formation of an inclusion complex nor preclude the addition of other components.

Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Examiner's hours, phone & fax numbers

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (571) 272-0656. The examiner can normally be reached on Tuesday, Wednesday, and Friday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson (571) 272-0661, may be contacted. The fax number for Group 1600, Art Unit 1623 is (703) 872-9306.

Visit the U.S. PTO's site on the World Wide Web at http://**www.uspto.gov**. This site contains lots of valuable information including the latest PTO fees, downloadable forms, basic search capabilities and much more.

Leigh C. Maier
Patent Examiner
May 11, 2004

SAMUEL BARTS
PRIMARY EXAMINER
GROUP 1600